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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,374	09/16/2003	Se-Jin Lee	JHU1800-3	5508

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,374	LEE ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *16-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/04, 11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a non-provisional of provisional application of 60/486,863 of 7/10/2003, 60/439,164 of 1/9/2003 and 60/411,133 of 9/16/2002.

The preliminary amendment filed on 9/16/2003 is acknowledged. Claims 1-66 are pending.

Applicant's election with traverse of Group I, Claims 1-15, drawn to a method of modulating activation of myostatin by modulating metalloprotease activity, which mediates activation of latent myostatin, by cleavage, and BMP- 1, as a species of protein in the response filed on 7/12/2006 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 16-66 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in communication filed on 7/12/2006.

Claims 1-15 are under consideration and are being examined herein.

Priority

Acknowledgement is made of applicants claim for US provisional application of 60/486,863 of 7/10/2003, 60/439,164 of 1/9/2003 and 60/411,133 of 9/16/2002.

Drawings

The drawings have been submitted on 9/16/2003 with this application.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 4/29/2004 and 11/21/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Objections

Claims 3 and 4 are objected to as encompassing non-elected subject matter. Appropriate correction is required.

Claims 1, 5 and 9 are objected to with recitation "pro peptide" should be either pro-peptide" or "propeptide". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a method of modulating any myostatin activation, comprising contacting a any latent myostatin complex comprising any myostatin pro-peptide and any myostatin C-terminal fragment, and any metalloprotease that can cleave the myostatin pro peptide, with an agent that increases or decreases proteolytic cleavage of the pro-peptide by the metalloprotease, thereby modulating myostatin activation. Claim 2 recites the method, wherein the metalloprotease is a bone morphogenic protein- 1/tolloid (BMP- 1/TLD) family member and claim 3 recites the method, wherein the BMP-1/TLD family member is BMP-1, TLD, tolloid-like protein-1 (TLL-1), or tolloid-like protein-2 (TLL-2). Claim 4 recites the method, wherein the BMP-1/TLD family member is BMP-1, mammalian TLD (mTLD), mammalian TLL-1 (mTLL-1), or mammalian TLL-2 (mTLL-2) and claim 5 recites the method, which comprises increasing myostatin activation, said method comprising contacting the latent myostatin complex and metalloprotease with an agent that increases proteolytic cleavage of the pro-peptide by the metalloprotease, thereby increasing myostatin activation. Claim 6 recites the method, wherein said contacting is performed on a sample in vitro and claim 7 recites the method, wherein the sample comprises a cell sample, a tissue sample, or a biological fluid sample. Claim 8 recites the method, wherein said contacting is performed in vivo, said method comprising administering the agent to a subject and claim 9 recites the method, wherein the agent decreases proteolytic cleavage of the pro peptide by the metalloprotease, thereby reducing or inhibiting myostatin activation. Claim 10 recites the method, wherein, in the subject, muscle mass is increased, fat content is decreased, or a combination thereof and claim 11 recites the method, wherein the subject is an animal raised as a food source. Claim 12 recites the method, wherein the animal is a mammalian species, an avian species, or a piscine species and claim 13 recites the method,

wherein mammalian species is an ovine species, a porcine species, or a bovine species. Claim 14 recites the method, wherein the avian species is a chicken or a turkey and claim 15 recites the method, wherein the subject is a human subject.

As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the structure of only several representative species of such agents, which modulate metalloprotease. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the identifying characteristics of the agent (peptide), which inhibits cleavage of latent myostatin. Given this lack of description of representative species encompassed by the genus of peptide used in the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of modulating activation of myostatin protein of SEQ ID NO:

2, by a metalloprotease of human BMP-1 that can cleave the myostatin pro peptide, with peptide agents such as SEQ ID NO: 9-23 that decreases proteolytic cleavage of the pro-peptide by the metalloprotease BMP-1, thereby decrease myostatin activation, does not reasonably provide enablement for a method of modulating any myostatin activation, comprising contacting any latent myostatin complex comprising any myostatin pro-peptide and any myostatin C-terminal fragment, and any metalloprotease that can cleave the myostatin pro-peptide, with any agent that increases or decreases proteolytic cleavage of the pro-peptide by the metalloprotease, thereby modulating myostatin activation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is so broad as to encompass a method of modulating any myostatin activation (any metalloprotease specific) by using any agent that increases or decreases proteolytic cleavage of the pro-peptide, thereby modulating myostatin activation. Claim 2 recites the method, wherein the metalloprotease is a bone morphogenic protein- 1/tolloid (BMP- 1/TLD) family member and claim 3 recites the method, wherein the BMP-1/TLD family member is BMP-1, TLD, tolloid-like protein-1 (TLL-1), or tolloid-like protein-2 (TLL-2). Claim 4 recites the method, wherein the BMP-1/TLD family member is BMP-1, mammalian TLD (mTLD), mammalian TLL-1 (mTLL-1), or mammalian TLL-2 (mTLL-2) and claim 5 recites the method, which comprises increasing myostatin activation, said method comprising contacting the latent myostatin complex and metalloprotease with an agent that increases proteolytic cleavage of the pro-peptide by the metalloprotease, thereby increasing myostatin activation. Claim 6 recites the method, wherein said contacting is performed on a sample in vitro and claim 7 recites the method, wherein the

sample comprises a cell sample, a tissue sample, or a biological fluid sample. Claim 8 recites the method, wherein said contacting is performed in vivo, said method comprising administering the agent to a subject and claim 9 recites the method, wherein the agent decreases proteolytic cleavage of the pro peptide by the metalloprotease, thereby reducing or inhibiting myostatin activation. Claim 10 recites the method, wherein, in the subject, muscle mass is increased, fat content is decreased, or a combination thereof and claim 11 recites the method, wherein the subject is an animal raised as a food source. Claim 12 recites the method, wherein the animal is a mammalian species, an avian species, or a piscine species and claim 13 recites the method, wherein mammalian species is an ovine species, a porcine species, or a bovine species. Claim 14 recites the method, wherein the avian species is a chicken or a turkey and claim 15 recites the method, wherein the subject is a human subject.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of agents broadly encompassed by the claims. The agents, which modulates metalloprotease specific myostatin cleavage could be a peptide encompassing the cleavage site of the myostatin protein or an inhibitor of metalloprotease, which requires a knowledge of and guidance with regard to which peptide or peptide derivatives of myostatin or which inhibitor of the metalloprotease to be used and detailed knowledge of the ways in which the peptide or peptide derivatives or unknown inhibitor structure relates to its function. However, in this case the disclosure is limited to the amino acid sequences of only a few peptides agents and a single representative myostatin protein.

The specification does not support the broad scope of the claims, which encompass a method of modulating any myostatin activation (any metalloprotease specific) by using any

agent that decreases proteolytic cleavage of the pro-peptide, thereby modulating myostatin activation and the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method of modulating any myostatin activation (any metalloprotease specific) by using any agent that increases or decreases proteolytic cleavage of the pro-peptide, thereby modulating myostatin activation. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any peptide agent that modulates metalloprotease-mediated activation of latent myostatin having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Lee et al. (US PGPUB 2002/0157126 A1, publication 10/24/2002, filing date 4/24/2001, claim priority of

60/054,461 of 8/1/1997). Lee et al. disclose a method of modulating a myostatin activation, comprising contacting a latent myostatin complex comprising a myostatin pro-peptide and any myostatin C-terminal fragment, and a metalloprotease that can cleave the myostatin pro-peptide, with an agent (peptides) that increases or decreases proteolytic cleavage of the pro-peptide by the metalloprotease, thereby modulating myostatin activation. Lee et al. also teach that said metalloprotease is BMP-1. Lee et al. further teach a method of increasing myostatin activation. Lee et al. furthermore teach the method, which comprise in vitro and in vivo methods of myostatin activation. Lee et al. also teach administering the agent to a subject wherein the agent decrease proteolytic cleavage of the propeptide by the metalloprotease, thereby increase muscle mass and decrease fat content in said subject, wherein the subject an animal raised as a food source, such as avian or piscine species or ovine, porcine or bovine species or chicken or turkey or a human subject. Therefore, Lee et al. anticipates claims 1-15 of the instant application.

Conclusion

Status of the claims:

Claims 1-15 are pending.

Claims 1-15 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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